AMERICAN JOURNAL OF PHARMACY.

PUBLISHED BY AUTHORITY OF THE

PHILADELPHIA COLLEGE OF PHARMACY.

HENRY KRAEMER, Ph.D., Editor.

Publishing Committee:

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VOL. 73. JULY, 1901. No. 7

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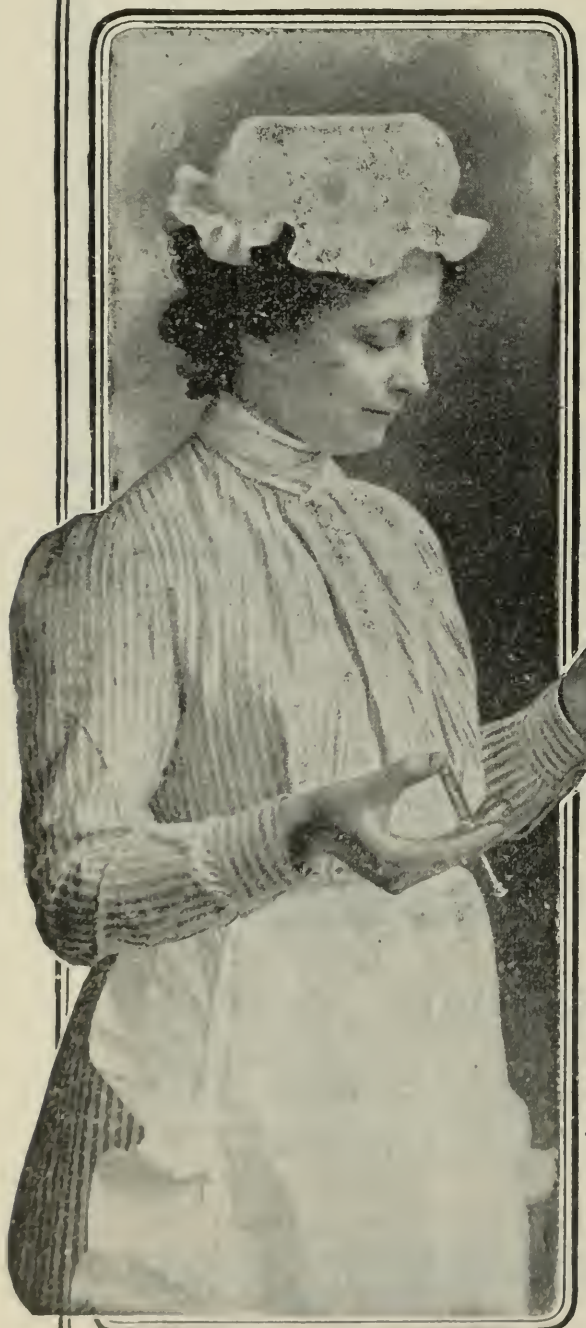

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THE AMERICAN
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JULY, 1901.

THE INTERNATIONAL PHARMACEUTICAL CONGRESSES.

By Fr. Hoffmann.*

At the annual meeting of a French pharmaceutical society held at Strassburg in August, 1864, the disadvantages of the constantly increasing manufacture of, and trade in, secret remedies (nostrums) was discussed and the desideratum expressed for counteracting and suppressing this growing and, as was claimed, dangerous evil in medication and pharmacy. A resolution was proposed and adopted for calling an international conference of delegates of the representative pharmaceutical associations for consideration and action in this matter.

It remains a matter of conjecture whether an invitation was extended by French pharmaceutical associations to other societies for arranging such a conference, or whether the resolution passed at the Strassburg meeting became known only by reports published in French, and subsequently republished in other pharmaceutical periodicals. The fact is that at the annual meeting of the General German Apothecaries' Association, held September 14–16, 1864, at Wiesbaden, about one month after the meeting in Strassburg, attention was called to the resolution passed there in regard to the nostrum trade. This resolution was submitted for consideration to a

* At the request of the Editor of this Journal I have, not without reluctance, consented to compile from a few American, British and German periodicals at my disposal this brief and incomplete retrospect upon the so-called international pharmaceutical congresses.

committee consisting of delegates of the North and the South German and the Austrian Apothecaries' Associations, and of the Pharmaceutical Society of St. Petersburg. This committee reported in favor of arranging an international conference for considering the prevailing nostrum evil and preparing a plan for proper and rigid restriction or suppression of the same. As a further topic for consideration it was suggested to come, if possible, to an agreement on a uniform strength of the pharmacopœial formulæ for commonly used galenical preparations of potent drugs, and to units of weights and measures.

This committee rendered at the same meeting the following report, which was unanimously adopted, and may have been the real impetus for the subsequent international pharmaceutical congresses:

"In Anbetracht, dass das Geheimmittel Unwesen mehr und mehr um sich greift, die Regelung der medicinischen Gesetzgebung unmöglich macht, und das Gesundheitswohl des Publikums gefährdet und den Ländern bedeutende Summen Geldes entzieht, erscheint es geboten, Mittel und Wege in Erwägung zu ziehen, wie diesem Unwesen Grenzen zu setzen und es gänzlich zu beseitigen sei.

"Die Würde des pharmaceutischen Standes und das Interesse desselben erfordern es, dass alle pharmaceutischen Vereine diese Bestrebungen kräftig unterstützen und an den bezüglichen Berathungen Theil nehmen. Um dieses zu ermöglichen haben die vereinten deutschen Apothekervereine in ihrer gemeinsamen Versammlung in Wiesbaden im September 1864 beschlossen, die sämmtlichen Apotheker Europa's zur Abhaltung eines internationalen Congresses einzuladen. Als Versammlungsort wählten die beiden deutschen Vereine, in vorläufigem Einverständnisse mit den in den Sitzunzen anwesenden Vertretern der Pharmaceutischen Gesellschaft in Sanct Petersburg und des Oesterreichischen Apotheker Vereins, die Stadt Dresden. Der allgemeine deutsche Apotheker Verein ist geneigt, seine Versammlung im nächsten Jahre dort ebenfalls abzuhalten.

"Nach den uns gemachten Mittheilungen ist die Beschickung des Congresses von Seiten der französischen Apotheker mit Sicherheit zu erwarten.

"Die Bestrebungen gebildeter englischer Apotheker, deren in der letzten Jahresversammlung des Oesterreichischen Apotheker Vereins Erwähnung gemacht wurde, lassen auch einer Betheiligung der Apotheker Englands entgegensehen."

Wiesbaden, d. 14 September 1864.

Dr. Rieckher, Oberdirector des Apotheker Vereins für Süddeutschland; *Dr. Geiseler*, für den Norddeutschen Apotheker Verein; *Dr. G. A. Björcklund*, für die Pharmaceutische Gesellschaft in Russland; *Klinger*, in Vertretung des Oesterreichischen ApothekerVereins.

In April, 1865, an invitation for and programme of, an international conference was issued, signed by the presiding officers (*Dr.*

Bley and *Dr. Geiseler*) of the North German and (*Dr. Rieckher*) of the South German Apothecaries' Associations. It contained the statement that at the last annual meeting of the General German Apothecaries' Association, held at Wiesbaden in September, 1864, a resolution had been adopted for arranging an international pharmaceutical congress, that this proposition meanwhile had met with the endorsement of other pharmaceutical societies at their meetings, and that the city of Brunswick had been chosen as place of meeting.

It was further stated, that the number of attendants should not be restricted, but that only delegates of recognized pharmaceutical associations would be entitled to voting, and that the deliberations will be conducted in the German language, while the use of French and English was also to be admitted.

The following queries were proposed for the consideration of the meeting:

(1) How and by what means can the professional position of the pharmacist be maintained?

(2) How can the insufficient supply of assistants be remedied to the advantage of both the employers and the employees?

(3) Are the benevolent funds instituted in support of sick and invalid assistants and of their widows, a success or a failure?

(4) What are the main disadvantages prevailing in maintaining the standing and the prosperity of the pharmacist?

(5) Would the principle of free competition extended to pharmacy improve the condition of the pharmacist and offer any advantage to the public?

(6) How can a uniformity of the formulæ of the pharmacopœial galenicals be attained?

(7) Is the universal introduction and adoption of the metric system in weights and measures desirable and what is the best way to bring it about?

(8) Should pharmacopœias invariably be written and published in the Latin language?

(9) How can quackery and the nostrum evil effectually be checked and suppressed?

(10) How is the sale of poisons to be regulated so as to prevent abuse dangerous to life and health, without at the same time making the useful application of poisons too difficult?

FIRST INTERNATIONAL PHARMACEUTICAL CONGRESS IN BRUNSWICK, 1865.

The *Congress* took place immediately after the annual meeting of the North German Apothecaries' Association in *Brunswick*, September 16 and 17, 1865. Only a few sessions were held and attended by twenty-nine delegates, representing twelve pharmaceutical societies of Germany, Austria, Russia, France and Sweden.

Mr. *Dittrich*, of Prague, was elected President and Mr. *Robinet*, of Paris, Vice-President.

The following conclusions were the result of the deliberations on the before-stated respective questions submitted to the Congress:

(1) By obligatory higher preliminary education and an adequate professional education consisting of three to three and a half years' apprenticeship (two to two and a half years for young men of superior preliminary education), of three years' service as assistant, and three terms of university or college study. The requirements at the State examination for obtaining the license as apothecary should be raised, particularly in inorganic and organic chemical analysis.

(2) By the same measures as proposed in the reply to the first question.

(3) No definite conclusion was obtained.

(4) Repression of the nostrum trade and the dispensing of medicines by medical practitioners.

(5) This question was answered in the negative. Experience demonstrates the fact that free competition has proved of rather detrimental consequences, nor is it conducive to cheapening the prices of medicines.

(6) At the periodical revision of the various pharmacopœias a uniformity of the formulæ should be gradually attempted.

(7) The desirability of the adoption of metric units was generally conceded, and the opinion prevailed that it should be made obligatory by governmental ordinances. The introduction would not cause any considerable difficulty or inconvenience.

(8) Generally consented as best and even necessary.

(9) The discussion of this question was a very animated one. The nostrum industry was declared unethical and discreditable. No government ought to permit this trade, detrimental to public and private health, nor protect by patent or trade-mark rights alleged or empirical medical discoveries when introduced as secret remedies or specialties. The pretended formulæ of the constituents of nostrums are mostly vague or incorrect, and the certificates for their efficiency fraudulent or obtained by bribes. The nostrum trade is based upon false pretenses, deceit and popular credulity, and should be repressed by all means.

Cosmetics should be placed under the control of the health authorities.

Even the French delegates endorsed these sentiments, stating that the French pharmaceutical associations recently had expelled from membership all makers of specialties, and that the great majority of French pharmacists discountenanced nostrums.

At the conclusion of the Congress a standing committee for selecting place and time and initiating the proper arrangements for holding a second Congress after the lapse of three years, was appointed, consisting of the presidents of the five principal pharmaceutical societies of the Continent,

The two pharmaceutical societies of Great Britain and the Ameri-

can Pharmaceutical Association, although invited in time, were not represented at this first International Congress. The Council of the Pharmaceutical Society of Great Britain rendered at its meeting, August 2, 1865, the following response to the invitation received:

"Whilst this Society estimates highly the proposed objects of holding an international conference of pharmacists, and would gladly give any facilities in its power to their prosecution, it is scarcely within its functions as a corporate body to appoint representatives thereto. We would, however, draw the attention of the Committee on Arrangements to a voluntary association existing in this country under the title 'British Pharmaceutical Conference,' one of whose objects is a correspondence with societies with similar aims in other countries, to whom such a communication may be addressed. This being done, the Pharmaceutical Conference would probably arrange, if practicable, to co-operate in some way at a future meeting."*

SECOND CONGRESS IN PARIS, 1867.

The committee elected at the Congress in Brunswick, selected Paris as the place for holding the second meeting and confided all arrangements to the Society of Pharmacy of Paris. The committee of this society addressed, early in 1867, an invitation to and programme for, the Congress to be held on August 21–25, 1867, at the time of the second World's Fair in Paris.

The programme argues "that pharmacy in Europe at this time is in an unhealthy and critical condition, not less injurious to the true interests of the public than to those of the profession itself. This critical situation has been explained by the Congress of Brunswick, and that body has given the results of its deliberations in the form of resolutions.

"In consonance with the present efforts of various countries to attain to an international uniform type in weights, measures, moneys, etc., the Congress will naturally be led to recognize the necessity of a code or legal formulary as a guide to the pharmacists of all countries. This code will insure uniformity of composition and strength in the commonly used medicines, particularly the more potent ones."

The Committee of Organization therefore proposes the following questions to be considered at the meeting of the Congress of 1867.

(1) What character should be attributed to the pharmacist? What are the functions he should perform and what conditions ought he to accomplish in order to acquit himself of his professional obligations?

**Pharmaceutical Journal and Transactions*, 1865-1866, p. 93.

(2) What are the most expedient ways and means of elaborating a code or formulary of official medicines, for which it is important to establish a uniform composition?

(3) What are the best and most practical means of determining the amount of active principles, especially of alkaloids in the drugs containing them, and in the galenical preparation of these drugs?

Each association will be entitled to three delegates, national associations to three delegates for every 100 of its members, but each delegation will have only one vote.

The Congress was attended by about fifty delegates from France, three from Holland, two from the United States (Wm. *Procter, Jr.*, of Philadelphia, and *John Faber*, then residing at Nuremberg), three from Germany, four from Austria-Hungary, three from Russia, two from Spain, two from Switzerland, one from Italy, one from Sweden and one from Egypt. *Dr. Rieckher*, of Germany, was elected President, with five honorary vice-presidents.

The deliberations seem to have been not strictly in the line of the proposed questions. The main discussions and resolutions related to the following subjects:

How can the status and prosperity of the practice of pharmacy be best advanced?—By restriction of the relative number of pharmacies and by a proper control and limitation in proportion to the number of inhabitants and the increase of population. The American delegates were the only ones who voted in the negative.

It was recognized to be advisable to institute pharmaceutical advisory boards for assisting the Government in the proper regulation and control of pharmaceutical and sanitary affairs. In this connection, a resolution was added, declaring that the trade in nostrums and trade-marked specialties and their advertisements in the newspapers should be strictly prohibited. The American delegates refrained from voting on this question.

The traditional problem of an international pharmacopœia caused a long but unavailing discussion. It was finally agreed that the Latin language was the best one for a universal code and that the elaboration of such a one should be undertaken. Only the delegates of the United States voted against this resolution for the reason that the broad differences of views in regard to many important galenical preparations in use in America, as well as in England, together with the numerous preparations and drugs used on the continent and not esteemed in America and England as meri-

torious, were obstacles too great to meet the approval of American and British pharmacopœia committees.

At the conclusion of the Congress, the Committee of Organization for a next Congress, appointed at the Brunswick meeting, was re-elected and Vienna proposed as place for assembling.

THIRD CONGRESS IN VIENNA, 1869.

The invitations and programme having been sent out early in 1869, the delegates to the Third International Pharmaceutical Congress convened in Vienna, September 9, 1869. The following countries were represented by delegates: Austria by twelve, Germany by nine, Russia by three, France by three, Italy by one, Switzerland by one, England by two (H. S. *Evans* and Theoph. *Redwood*) and the United States by one (John *Faber*, of Nuremberg). Mr. Wm. *Dankworth*, of Germany, was elected President and Messrs. *Robinet*, of France, and *Trapp*, of Russia, Vice-Presidents.

The questions submitted to the Congress were:

(1) Are independent schools of pharmacy desirable?—The delegates of the various countries briefly described the collegiate education at home. They finally agreed upon the resolution that higher pharmaceutical schools, as an integral part of universities, with pharmacists as professors in the classes relating exclusively to pharmacy, would be preferable in the interest of both the public and the profession.

(2) What advantages will arise from syndical chambers proposed at the preceding Congress?—The committee to whom this query had been submitted reported in favor of establishing such syndical chambers as representative and advisory bodies between the pharmaceutical association and the Government. They might be formed of delegates from the pharmaceutical corporations within certain districts. Their duties would consist in representing the profession in forming new regulations affecting pharmacy, and in acting as executive bodies for the proper working of existing laws.

(3) Is the supremacy of the medical profession in regulating pharmaceutical matters compatible with the present professional and social standing of the pharmacist, and does it conduce to the interests of the State, the public and the pharmacist?—This question applied to pharmacy in continental Europe only. The delegates shared in the opinion that the scope and the extent of medical knowledge

have reached such an amplitude that medical men on the average cannot any more enter upon the study of pharmaceutical branches, that, therefore, the pharmacist should replace the physician in the conduct and regulation of purely pharmaceutical affairs. If the governments have any doubt in their professional ability to do so, they should raise the standard of pharmaceutical education and the requirements at the State examinations.

(4) What should be done to attain to the greatest possible uniformity in the composition and strength of the pharmacopœial preparations?—It was stated that the Pharmaceutical Society of Paris had volunteered to undertake the compilation of a comparative conspectus showing side by side the differences existing in the various pharmacopœias in regard to the composition and relative strength of the identical galenical preparations in the various countries in order to initiate steps to have the pharmacopœias adopt uniform formulæ in course of time. This work has been commenced and will be submitted to the next Congress.

(5) What methods are best for assaying the organic alkaloidal drugs?—This question was dropped as hardly pertaining to the present objects of the Congress. It was, however, acknowledged that the methods for ascertaining the proportion of the active principles of drugs prescribed in the pharmacopœias needed improvements and that this matter belonged to the domain of the committees of pharmacopœial revision.

In conclusion it was resolved that the President may prepare a report on the resolutions of the Congress and communicate this report to the governments of those countries who were represented by delegates.

The proposition was made and endorsed to hold the fourth International Pharmaceutical Congress after the lapse of three years. The presidents of the National Pharmaceutical Associations of Austria, Germany, Russia, and France were delegated as a committee for selecting the place of the meeting and making in time, the proper arrangements for such a meeting. The delegate from Russia tendered an invitation to hold this in St. Petersburg.

THE FIRST MOVE TO INVITE THE CONGRESS TO HOLD A MEETING IN THE UNITED STATES OF AMERICA.

In consequence of the Franco-German war in 1869 and 1870 the

holding of the fourth Congress within the time stipulated at the preceding meeting in 1867 was delayed for two years. Meanwhile an initiatory move was made by Professor *Maisch* and endorsed by President *E. H. Sargent* in his presidential address before the annual meeting of the *American Pharmaceutical Association* held in Baltimore, Md., in September, 1870, for holding the fifth Congress in Philadelphia in the Centennial year, 1876. This proposition met with approval and a committee consisting of Messrs. *Wm. Procter, Jr.*, *Albert E. Ebert* and *Fred. Hoffmann* was appointed to report on the subject with a plan of action, at the meeting of the Association in 1871.

This committee presented the following report to the American Pharmaceutical Association at its meeting in St. Louis, September, 1871:

That in view of the notable period in the history of our country, the Centennial anniversary of its political independence, which will be reached in the year 1876, we are called upon, in common with all citizens of the Republic, to manifest our patriotic impulses in a worthy manner, by showing the advancements made in the arts and sciences, and the progress towards a higher civilization. Further, as at that time unusual inducements and attractions will doubtless cause many to visit this country from foreign lands, it is believed that so favorable an opportunity will not soon occur again to bring together in this country pharmacists of Europe.

It is therefore recommended that the International Pharmaceutical Congress be solicited to postpone the meeting which would occur in its regular order in 1875, and that this Association extend a cordial invitation to that body to meet in this country in the year 1876. But if for any reason the Congress should deem it not advisable to accept such invitation, it is recommended that an invitation be extended to the delegates present at the meeting in 1872, and to the pharmacists of all nations, to meet with this Association in 1876.

Your committee further recommends, that at the present meeting the month of July and the city of Philadelphia be designated as the time and place for the meeting of 1876, it being manifestly appropriate that the meeting of that year should be held in the centre of pharmaceutical and political interest, and in the month dedicated to the celebration of our National Independence. The action recommended seems necessary at this time, in order that our annual meetings intervening may be located in view of such decision, and that appropriate efforts may be made to insure at that meeting a full representation of American pharmacists, thereby making this association a truly national brotherhood of all engaged in our noble profession.

Your committee further recommends the appointment of a committee at this meeting for devising suitable plans and recommending such preliminary arrangements as seem necessary to render the meeting of 1876 worthy of the occasion.

[Signed] ALBERT E. EBERT.
FRED. HOFFMANN.

Professor *Procter* refrained from signing this report on account of the fact that the International Congresses thus far have only devoted themselves "to correcting abuses that exist in Europe in the laws bearing on the profession there. By transferring their delegates to this country, to act here just as they do there, would be unpracticable and unavailing in consideration of the very different views and usages prevailing in the practice of pharmacy in the United States and England."

At the meeting of the American Pharmaceutical Association in St. Louis, September, 1871, it was, however, stated that, although all the discussions of the International Congresses thus far held amounted to very little to American pharmacists, inasmuch as they naturally had been discussing subjects of particular interest and application only to the country in which they met. If they should come here where the conditions under which pharmacy is practised are essentially different from those existing in Europe, the questions to be discussed and the deliberations would undoubtedly be pertinent to and in accordance with these conditions.

The report of the committee and the motion to invite the International Pharmaceutical Congress to meet in the United States in 1876 was unanimously adopted with but two dissenting votes, and the city of Philadelphia was chosen as place of meeting.

In compliance with these resolutions the following invitation was addressed, July 13, 1874, by the *American Pharmaceutical Association* to the fourth International Pharmaceutical Congress at St. Petersburg:

* * * In the year 1876 occurs the one hundredth anniversary of the Independence of the United States of America. This historical event will be celebrated throughout our country, and an international industrial exposition will be held in the city of Philadelphia. * * *

It is more than probable that this Industrial Exposition will be visited by many European pharmacists, and that this occasion will be a fit and convenient opportunity to unite the delegates of the pharmaceutical societies, throughout the civilized world, in council on the questions affecting the present and future status of pharmacy among the nations, or having a practical or scientific importance for our profession.

The officers of the American Pharmaceutical Association, in carrying out the resolution of this association adopted at its meeting in St. Louis in 1871, cordially invite the fourth International Pharmaceutical Congress to appoint the year 1876 and the city of Philadelphia as the time and place of meeting of the fifth Congress.

* * * Should the fourth Congress deem it inexpedient to call the fifth Congress to meet in the United States in 1876, we now invite all the societies which may be represented at the St. Petersburg Congress, and all pharmacists, to meet the American Pharmaceutical Association at its twenty-fourth annual meeting, which will be held in Philadelphia during the International Industrial Exhibition in 1876.

[Signed] JOHN F. HANCOCK,
President.

JOHN M. MAISCH,
Permanent Secretary of the Amer. Pharmac. Association.

This letter of invitation was laid before the Congress at St. Petersburg, as stated further on. As no response had been received from the presiding officers of the Congress until nearly one year after the letter had been sent, the Permanent Secretary of the American Pharmaceutical Association addressed, on June 3, 1875, the following inquiry to the President of that Congress:

The American Pharmaceutical Association will hold its twenty-third annual meeting in Boston early in September, 1875, and will then determine upon the proper measures for its twenty-fourth meeting, which will convene in Philadelphia during the International Exhibition in 1876. You are aware that the fourth International Pharmaceutical Congress was invited to call the meeting of the fifth Congress to assemble in Philadelphia in 1876. The selection of the proper place and time having been referred to the International Congress Committee, I take the liberty of inquiring of you whether that committee has decided upon the invitation above referred to.

I also beg to ask for information in relation to the proposed draft of an international pharmacopœia; if possible, the American Pharmaceutical Association desires to participate in its elaboration.

[Signed] JOHN M. MAISCH,
Permanent Secretary, A.Ph.A.

PHILADELPHIA, June 3, 1875.

It seems that no reply has been received to this letter neither. This ended the first effort of inducing the Congress to hold a meeting in the United States during the Centennial year 1876.

(*To be continued.*)

THE LOWERING OF THE TEMPERATURE OF WATER of maximum density by solutions of various salts is shown by de Coppet (*Compt. rend.*, May 20, 1901) to be proportional to the quantity of the substance dissolved and that with the exception of lithium salts the molecular lowering is almost constant.

RECENT DEVELOPMENTS IN THE STUDY OF THE RELATIONSHIP BETWEEN CHEMICAL CONSTITUTION AND PHYSIOLOGICAL ACTION OF ORGANIC COMPOUNDS.

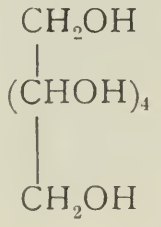
By Prof. Virgil Coblentz.

(*Concluded from p. 272.*)

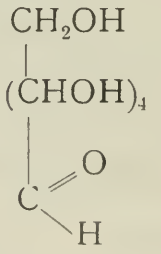
RELATIONSHIP BETWEEN TASTE AND CHEMICAL CONSTITUTION.

Sweet and bitter taste has long played a very important part in modern medicine and pharmacy. Formerly resort was always had to the use of corrigents. However, of late years, synthetic chemistry has endeavored to solve this question from a purely scientific standpoint, through the introduction of certain groups which would not interfere in any manner with the therapeutic effects of the original substance.

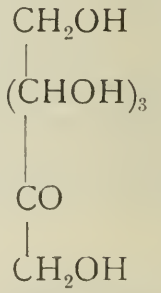
In alcohols of the aliphatic series the sweetness increases to a certain extent with the number of entering hydroxyl groups, as for example, the glycols, glycerol, mannitol. The polyhydric alcohols are less sweet than their corresponding aldehydes and ketones, as for example, mannitol and its aldoses and ketoses.



Mannitol.



An Aldose.



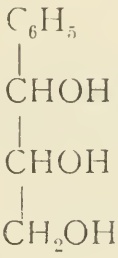
A Ketose.

According to W. Sternberg, the hydroxyl (OH) and amido (NH_2) groups are taste generators, the entrance of one hydroxyl carries odor and two or more taste. The presence of a carboxyl group produces in all cases a sour taste. Stereo geometrical configurations play no part. This investigator also claims that a certain harmonic relation between the substituting hydroxyl and the substituted alkyl groups is necessary for the development of sweet taste. Every alkyl group must stand opposite a hydroxyl, as is the case in glycerol and mannitol. The alkyl groups may be permitted to exceed the hydroxyls by one member only, so that the

molecule contains one oxygen less than carbon without the sweet taste suffering, for this reason the disaccharides (sucrose) are sweet and the tri and poly-saccharides are tasteless.

On replacing the alkyl radical in glucoses by a phenyl, an intense bitter substance results.

Butenyl Glycerol
Sweet.

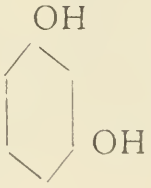


Phenyl Glycerol
Bitter.

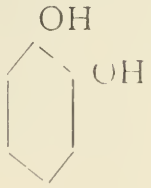
The natural glucosides are bitter because they are mostly phenol derivatives.

Symmetry of the hydroxylated compound is also necessary, thus those di and tri-hydric phenols whose substituting groups occupy the symmetrical meta position are sweet, for example:

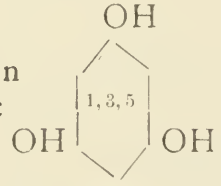
Resorcin
m-dioxy-benzole
sweet



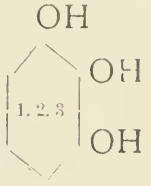
Pyrocatechin
o-dioxy-benzole
bitter



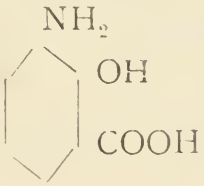
Phloroglucin
symmetric
sweet



Pyrogallol
bitter

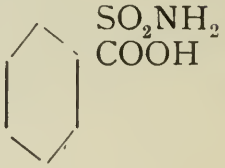


The amido group (NH_2) lends a sweet taste to hydrocarbons under the conditions that a negative carboxyl group (COOH) is present and the other groupings are closely linked thus the ortho amido-salicylic acid is feebly sweet, while the para acid m ta compounds are tasteless.

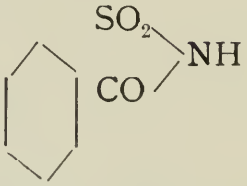


Ortho-amido-salicylic acid

Amido-benzoic acid loses its sweet taste through the introduction of an extra acid group and only in

Ortho-sulfamid-benzoic acid 

through the close linkage brought about by the andride formation is an intense sweet taste developed



Ortho-benzoic sulfinid.

To correct taste, efforts are generally directed toward either closing the reactive groups through the addition of radicals or the conversion of the substance into an insoluble compound which, however, must be of such a nature as to readily split up in the alkaline secretions of the intestinal canal. Efforts to render quinin salts tasteless have been successful in such combinations as quinin chloro carbonic ester CO . Cl . $C_{20}H_{23}N_2O_2$, also Euchinin—an ethyl carbonic ester of quinin C_2H_5O — CO — $OC_{20}H_{23}N_2O_2$

Freedom from tinnitus as well as from taste is claimed for these salts.

The tasteless character of quinin tannate is known to us all. The disagreeable taste and undesirable action in the stomach produced by tannin are repressed by forming an insoluble compound with albumen, casein or gelatin, as for example in such compounds as Tannalbin (a compound of tannin and albumin), Tannigen (acetic ester of tannin), Tannon (a condensation product of tannin and urotropin), Tannoform (a condensation product of tannin and formaldehyde). These are all valuable intestinal astringents. In this connection the salol class of intestinal antiseptics introduced by Nencki may be mentioned. Here not only the taste but also the caustic action of many substances is avoided through esterification.

Salol $C_6H_4\begin{matrix}OH\\COOC_6H_5\end{matrix}$ *Phenyl salicylic ester.*

Betol $C_6H_4\begin{cases}OH\\COO-C_{10}H_7\end{cases}$ — *Salicylic napthyl ester.*

Salacetol $C_6H_4\begin{cases}OH\\COO-CH_2COCH_3\end{cases}$ — *Salicyl acetol.*

Salophen $C_6H_4\begin{cases}OH\\COO\cdot C_6H_4\begin{cases}NH\\COCH_3\end{cases}\end{cases}$ — *Aceto-para-amido-salol.*

Cresalols $C_6H_4\begin{cases}OH\\COO\cdot C_6H_4CH_3\end{cases}$ — *Salicylic-cresylic esters.*

As esters of Guaiacol

$$C_6H_4\begin{cases}OH\ (1)\\OCH_3\ (2)\end{cases}$$

we have the valuable comparatively tasteless and less disturbing compounds

Duotal $CO\begin{cases}O-C_6H_4OCH_3\\O-C_6H_4OCH_3\end{cases}$ — *Guaiacol carbonate.*

$C_6H_3\begin{cases}OH\\OCH_3\\COOH\end{cases} + 2H_2O$ — *Guaiacol carbonic acid*

Benzosol $C_6H_4\begin{cases}OCH_3\\O-C_6H_5CO\end{cases}$ — *Guaiacol benzoate.*

Styracol $C_6H_4\begin{cases}OCH_3\\O-C_6H_4-CH=CH-CO\end{cases}$ — *Guaiacol cinnamate.*

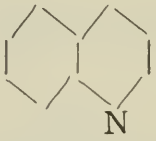
Geosote $C_6H_4\begin{cases}OCH_3\\O-COCH_2-CH=(CH_3)_2\end{cases}$ — *Guaiacol valerate.*

Guaiamar $C_6H_4\begin{cases}OCH_3\\O-CH_2-CHOH-CH_2OH\end{cases}$ — *Guaiacol glyceryl ether.*

ANTIPYRETICS.

Formerly the efforts of the synthetic chemist were directed toward producing bodies analogous in character and action to the well known quinin. Ten years ago the views as to the constitution of quinin were

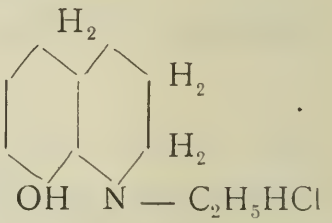
erroneous, hence such synthesized substances differed essentially from this alkaloid. Of all the synthetic antipyretics none possess the most important function of quinin, that is, its specific action in malaria. Quinolin



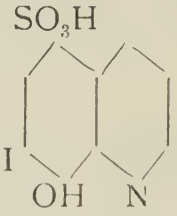
being the mother substance of quinine, was necessarily the basis of these attempts. Filehne found that only the alkylated nitrogen of a tetrahydro quinolin was worthy of trial; following this came Fischer's Kairin, Kairolin and Skraup's Thalline

Kairin

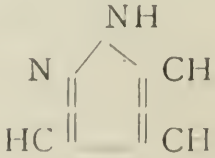
(ethyl-ortho-oxy-quinolin tetra hydride).



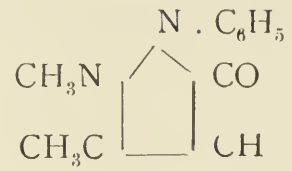
Owing to the unpleasant and sometimes dangerous toxic side actions this class of derivatives has been dropped. This nucleus furnishes us, however, a valuable antiseptic in Loretin (meta-iodo-ortho-oxy-quinolin-ana-sulfonic acid).



With the intention to produce a quinine-like body Knorr discovered antipyrin. This investigator's views as to the constitution of this synthesized body were at first erroneous. Knorr thought that this newly discovered body was a di-methyl-oxy-chinizin in which two quinolin molecules were linked to the pyridin nucleus, as was supposed to be the case with quinin. Later it was found that the five-membered ring Pyrazol

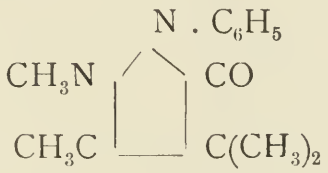


was the nucleus, antipyrin being a phenyl 1 — dimethyl 2, 3 — pyrazolon 5.



Tolypyrin resulting through the introduction of a methyl group possesses a more irritating action, 4 grammes bring equivalent to 5 to 6 of antipyrin.

The only active competitor of antipyrin belonging to this series was found in Pyramidon, a di methyl-amido-antipyrin which is three times as active as antipyrin



ANILIN DERIVATIVES.

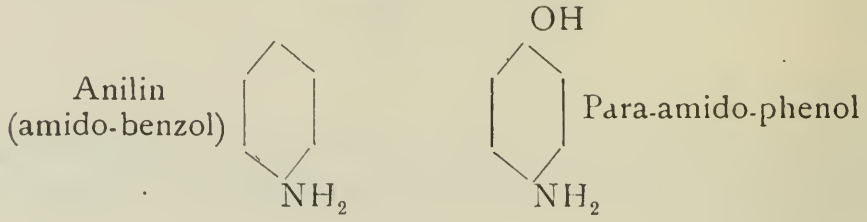
The accidental discovery of the antipyretic and anti-neuralgic properties of acetanilid led to its study and subsequent unlimited application in the preparation of innumerable medicinal derivatives. The introduction of acid radicals in place of a hydrogen of the amido group of a base results in the diminution of its toxic action on the ground that the substance has become more resistive to the decomposing action of the body fluids; hence acetanilid $C_6H_5NHCH_3CO$ represents the toxic characters of anilin but in a milder degree, its action being that of anilin in a weak and protracted condition.

Benzanilid $C_6H_5NHC_6H_5CO$ splits up with difficulty and slowly in the system, hence its action is milder than that of acetanilid. Salicylic anilid fails to break up, hence is without action.

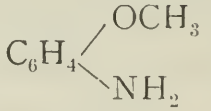
PARA-AMIDO-PHENOL DERIVATIVES.

With the experience of acetanilid and its derivatives synthetic chemists made systematic efforts to build up a substance which should represent the antipyretic and antineuralgic properties of acetanilid without its unpleasant side effects and action on the hemoglobin of the red blood-corpuscles.

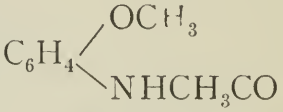
The investigations of Schmiedeberg demonstrated that anilin was altered and rendered less toxic in the organism through oxidation in the para position yielding para-amido-phenol.



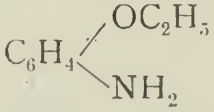
With this in view, also that para amido phenol was less toxic than anilin, an acetyl radical was introduced with the hope of obtaining an ideal antipyretic. The resulting acetyl para amido phenol still possessed toxic antipyretic symptoms, hence it was found necessary to close or protect the free hydroxyl group through the introduction of an alkyl radical. If a methyl group is employed, methacetin results; an ethyl, phenacetin; other alkyls, as propionyl, butyryl, etc., have been employed in place of the ethyl, but the resulting compounds, because of their great insolubility, react too slowly in the system.



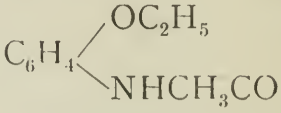
Anisidin



Methacetin



Phenetidin



Phenacetin

The maximum of antipyretic and antineuralgic action is found in the methyl derivative (methacetin), while the least toxicity is possessed by the ethyl derivative (phenacetin). The readiness with which the acid secretions of the stomach split off the acid rest preparatory to the decomposition of the resulting phenetidin nucleus depends largely upon the nature of the acid employed. Among these derivatives in which the acetic acid rest of phenacetin is replaced by other acid rests are lactic (Lactophenin), valeric (Sedatin), salicylic (Salophen), phenyl glycolic (Amygdophenin), vanillic (Vanillin-p-phenetidin), etc.

Each of these possesses slightly different characters as regards solubility, rapidity of action, varied elimination of toxic effects, etc.

Owing to the insolubility of phenacetin, one of the earliest endeavors was to obtain a compound sufficiently soluble to enable its employment in solution. This was accomplished by the addition of a basic group, glycocoll (amido acetic acid), which, through its amido group, is capable of uniting with other acids and forming very soluble salts.

Phenocoll $C_6H_4 \begin{cases} OC_2H_5 \\ NHCH_2NH_2CO \cdot HCl. \end{cases}$

Amido-acet-para-phenetidin hydrochlorid. The soluble salts are the hydrochlorid, acetate and salicylate (Salocoll).

All antipyretics act in a greater or lesser degree on the blood in which the oxyhæmoglobin is converted into methæmoglobin and the respiratory capacity lessened and the red blood-corpuscles modified, the blood pigment at times being set free.

According to Schmitt these remedies may be divided into the following classes:

(1) Antipyretics, which in moderate doses oxidize the hæmoglobin, as antipyrin and phenacetin.

(2) Remedies which in moderate doses fix the methæmoglobin within the blood-corpuscles as thallin, antithermin, kairin, exalgin, methacetin, acetyl amido-phenol.

(3) Remedies which fix the methæmoglobin, destroy the red corpuscles and set free the methæmoglobin which appears in the urine, for example, acetanilid, benzanilid, formanilid, pyrodin, etc.

The ideal antipyretic and antineuralgic with a specific antimalarial action has not as yet been found, and will not until either accident or a more accurate knowledge of the structure of quinin furnishes the means.

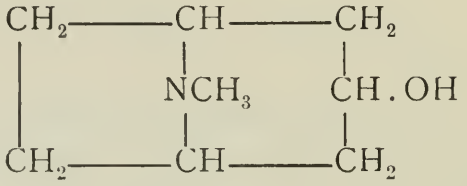
LOCAL ANÆSTHETICS.

On hydrolizing cocain with mineral acids, methyl alcohol and benzoic acid with the nucleus Ecgonin result, neither possesses local anæsthetic action.

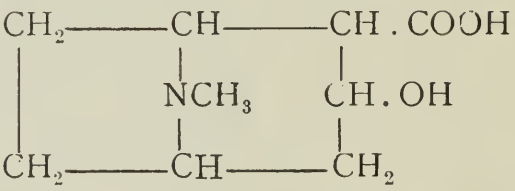
It does not matter which alkyl radical replaces the methyl of the $COOCH_3$ group, the homologue retains the typical properties of cocain.

Of greater importance is the replacement of the benzoyl group in cocain by other acid radicals, the anæsthetic properties are either lessened or disappear entirely.

Filehne thought that the benzoic acid rest was necessary, on the ground that atropin, Homatropin and the benzoic derivatives of other alkaloids, as morphin, hydrocotarnin and quinin, possessed local anæsthetic action.



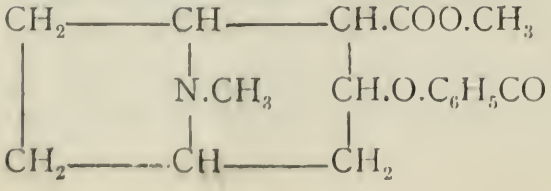
Tropin



Ecgonin

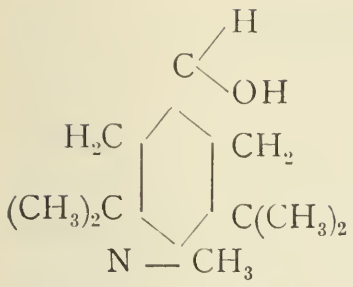
For the development of the action of cocain the position and union of the OH and COOH groups are of great importance, hence the stereo chemical configuration of the ecgonin nucleus is essential in conjunction with the anchoring benzoyl group. The methyl group covers the acid and irritating characters of ecgonin.

Further, the derivatives of tropin, which do not contain a carboxyl, the addition of a methyl group is not essential for action. On the other hand, the presence of an esterized carboxyl increases activity. The mydriatic effect stands likewise in close relationship to the fundamental base (a pyrrolidin), but the localizing action is governed only by aromatic acid radicals, as is the case in atropin and homatropin. Based on the view of Merling, that cocain was made up of two ring nuclei, and that one, a *methylated piperidin*, was the active base, several products were synthesized from the methylated base triaceton alkamin, namely

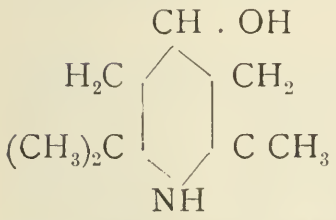


Cocain

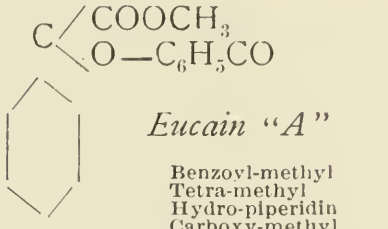
Benzoyl-methyl-ecgonin



Triaceton alkamin.

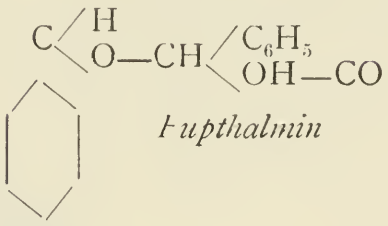


Vinyl diaceton alkamin.

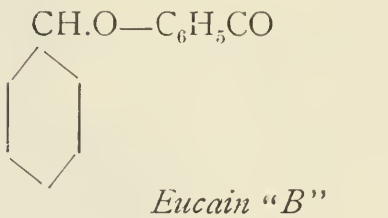


Eucain "A"

Benzoyl-methyl
Tetra-methyl
Hydro-piperidin
Carboxy-methyl
Ester.



Eupthalmin



Eucain "B"

the local anæsthetics eucain "A" and eucain "B" and the myotic euphthalmin

Eucain A, which is closely related to tropa cocain, is a local anæsthetic, it does not produce a dilation of the pupil, however, its irritating action on mucous surfaces are detrimental to its use. More successful as a substitute for cocaine was Eucain "B," which is free from irritating action and more active and less toxic than the former. Chemically, eucain "B" is the benzoyl derivative of the base vinyl-diaceton-alxamin, and like cocain, it loses its local anæsthetic effect on replacing the benzoyl radical with an acetyl. If a mandelic acid radical (C_6H_5—CH(OH)CO) is introduced in place of the benzoyl of eucain "B," the very active mydriatic eupthalmine results. The hydrochlorid of this base has chemically the same relation to eucaine "B" as homatropin has to tropa-cocain, that is euphthalmin is the hydrochlorid of the mandelic acid derivative of eucain "B."

Einhorn and Heinz have prepared various derivatives of the other half of the ecgonine complex, namely hexa-hydrobenzole. They found that all the esters of the aromatic hydroxy-amido acids possessed local anæsthetic properties, particularly so the methyl ester of para-amido-meta-oxy-benzoic acid ($C_6H_3(OH)(NH_2)COOCH_3$) which is called *orthoform.*

THE STORY OF THE PAPAW.

By F. B. Kilmer.

(*Continued from page 285.*)

THE MILK OF THE PAPAW.

Trees that give milk are plentiful in the tropics. The native name for the papaw is "lechoso" (a producer of milk). When an incision is made in the bark of any part of the tree or in the fruit rind, a limpid, milk-like liquid exudes very freely. It is slightly more dense than water, and in contact with the air quickly coagulates and closes the incision. This coagulation is a rather notable phenomenon.

For the fraction of a minute the liquid flows as though a milk bottle were uncorked, and one imagines that gallons will run without stopping, but suddenly it ceases. On examination it is found that the milk is coagulated for a considerable distance within the glands. I am quite firmly convinced that this action is due to the presence of a clotting enzyme. This assumption is made probable by the fact of the quite universal presence of pectin in plants, and further from the fact that I have proven the presence of calcium salts and pectic compounds in the latex of the papaw. This statement is further strengthened by my observation that the latex of the papaw will coagulate the juice (neutral or alkaline) of certain other plants. The presence of rennin ferment in the latex of the papaw is noted elsewhere in this paper. Its behavior is, in many respects, unlike that of the jelly-forming enzyme here noted, and, while further examination of fresh material is needed before making any fuller statement, I think I am safe in announcing that we may add the papaw latex to the list of plant juices in which the pectase ferment has been noted.

The odor of the fresh milk is pronounced, and not unlike that of the latex of the india-rubber tree, and, on the whole, is a disagreeable one, suggestive of decayed meat. The taste is somewhat bitter, rather markedly astringent and acrid. When dried by artificial heat the ferment power is weakened or lost, if dried in the sun it retains its activity and about 75 per cent. of moisture is separated.

This milky emulsion seems to be secreted for the most part in fairly large vessels (readily observable by a pocket lens), which lie just under the epidermis in every part of the plant. In the ripened

fruit it seems to permeate to all parts of the fleshy portion of the fruit (somewhat changed in character). The supply of milk in a vigorous tree is very abundant. After making several prolonged incisions in a single fruit, I estimated that an entire tree must contain several hundred ounces, but no such amount can be obtained by any practical method.

The dried milk of the papaw is an article of commerce, and its character is dependent upon the method of preparation. The main source is the crude method of the natives. The usual proceeding

Selling papaw fruit in the market.

is to make an incision just through the rind of the green fruit; the milk flows freely for a short time; this is caught in a dish, coagulation follows closely, and the milk oozes slowly through the incision for twenty-four hours or more. If numerous incisions are made in the fruit, it will, at the end of this time, become ½ an inch thick. The milk is most abundant after heavy rainfalls, from the first fruits of the tree, and naturally so from vigorous plants.

The latex, when allowed to dry on the fruit, becomes discolored

and dark. The lighter-colored and best products are produced when the coagulated juice is removed as fast as it exudes, spread out thin and quickly dried.

No advantageous method of gathering the milk has come under my observation. Some of the difficulties of the present usages can be imagined by the recollection that in some cases the fruits are from 20 to 30 feet from the ground. The coagulation allows only a small yield, requiring constant climbing to make fresh incisions. The latex yields 25 per cent. of dried material (still containing 6 to 10 per cent. of moisture). Under favorable conditions I extracted 100 grammes of latex from one fruit. One gatherer claimed an average yield of one pound of dried milk from each tree per year, though under somewhat adverse conditions it required fifty trees to yield one pound of dried milk.

OFFICE OF THE MILK AND ENZYME.

The office of this milk in the economy of the papaw is not easy to explain. Parkin (*Pharmaceutical Journal*, 1578, page 337) states: "The most important function of such a latex is that of holding water in reserve." This seems hardly possible in respect to this plant because all tissues of the plant are filled with a watery fluid, so much so that they flow upon cutting, and it is hardly possible that the tree is dependent upon the milky juice for a supply of moisture. The native observers suggest that the milk has to do solely with the ripening of the fruit, and it is true that as the fruit ripens it is in all parts permeated with the milk, and as a consequence the starch compounds are changed to sugar; the proteids are peptonized and the flavor mellowed. But it would seem to be a prodigious waste of energy if this ripening action was the only action of the milk and its enzyme contents.[11]

We do know, however, that this latex is the carrier of enzymes, and that in plant life certain enzymes play an important part in incorporating material for the growth of the living substance or of preparing material brought to it, so that it may be capable of such incorporation. Again, they bring about decompositions which

[11] Assuming that there is at the lowest estimate, 100 ounces of latex in a tree, we would have twenty ounces of dried material capable of converting about 3,000 pounds of proteids.

supply the energy needed for the maintenance of vital processes. In other words, these enzymes digest and prepare food for plant life and growth.

J. Reynolds Green has shown that in the process of nutrition in plants, when the constructive processes are active, an excess of material is elaborated and deposited in temporary reservoirs. This material is utilized by a process of digestion brought about by the agents of enzymes or ferments which are formed to digest these deposited materials. From many plants we have been able to separate diastasic, proteolytic, glucosidal, emulsifying and other ferments.

The papaw is a plant of quick growth. It rapidly appropriates and converts decaying vegetation. Its best fertilizers have been found to be dead vegetable and animal matter, house waste, etc. This suggests that the presence of this abundance of enzymic power is necessary for the digestion and conversion of plant-food material, and that the material is prepared for incorporation in the living plant by the enzymes present in the latex.

The milky juice of the papaw can therefore be imagined as quite akin to the gastric or pancreatic juice of the animal organism. The ducts through which this latex flows are possibly digestive tracts; their contents, an emulsion of partially digested proteid and other material, under transformation preparatory to ultimate assimilation.

Corrosive Properties of the Latex.—The corrosive action of the latex has been recorded; all species have this property in some degree. Persons who handle the green fruit in the preparation of pickles are troubled with raw and bleeding fingers and are forced to abandon the work. The fresh latex will irritate the mucous membrane and its continuous use is in some instances very escharotic. This property seems more manifest in certain isolated plants of apparently the same species. This is true not only of the Carica papaya, in universal cultivation by the natives, but also in other varieties the fresh juice will blister and cauterize almost instantly. A caustic property is not unusual in many tropical plants. In the milk of the papaw it is not due to acid constituents, as it is still present if the slight acidity is neutralized. It can be removed by chloroform and ether, and is either removed or destroyed in some of the processes of separating the ferments (precipitation).

The corrosive constituent is not volatile and remains in the dried juice. An examination of many of the preparations sold in our market under the name of "papain," etc., shows that this corrosive property had not been altogether removed.

ANALYSIS OF PAPAW LATEX.[12]

This latex is an emulsion of fats and wax, containing also extractive matters, albumen and salts, as shown by the following:

CARICA LATEX—SUN-DRIED.

Moisture	6·06
Soluble ash	2·64
Insoluble ash	4·78
Matters soluble in water (including ash)	82·74
" " " benzine	11·43
" " " ether	9·77
" " " chloroform	11·20
" " " acetone	5·98
" " " alcohol	7·16

ASH.

Total ash	7·42
Soluble ash	2·64
Insoluble ash	4·78
Calcium sulphate—insoluble ash	0·896
Calcium phosphate " "	3 72
Silica " "	0·164
Calcium sulphate—soluble ash	1·024
Potassium, sodium, lithium, chlorides and carbonates—soluble ash	1·616
Chlorine	0·22
Ferric oxide	trace

Alcoholic extract (7·16 per cent.) is colored, astringent and has a somewhat acrid taste. The concentrated extract is dark brown, resembling well known solid extracts. Evaporated residue is only slightly soluble in ether and chloroform, but is partially so in a cold 5 per cent. solution of sodium hydrate. It is further dissolved upon heating. Alcohol added to this sodium hydrate mixture dissolves it completely. Acid added to the aqueous or alcohol alkaline mixture gives a saponification indicating resins.

Some observers have reported a glucosidal body in the Carica latex. The usual tests for such substances, when applied to this

[12] Owing to the length of this paper, the detailed methods of analysis have been omitted. In most cases the methods were those in common use.

extract, give negative results. In my hands this extract gave no indication of tannin, although this substance has been reported as present in the milk. The acrid resins of the papaw are more or less extracted by alcohol, but more completely by acetone. The alcoholic extract is acid to litmus.

In this alcoholic extract the presence of an indicator was observed. When the extract is somewhat concentrated, the color becomes a beautiful pink which is destroyed by sodium hydrate, added to saturation, and upon concentrating the solution to dryness. The color is not restored by hydrochloric acid. (This color substance needs further study.)

Ether extract (9·77 per cent.) is nearly colorless, yielding upon evaporation a residue resembling white beeswax. This residue is quite soluble in chloroform, but only partially soluble in benzine or alcohol. (Soluble in hot alcohol.) The aqueous washings of this extract give an acid reaction with litmus and a precipitate with lead acetate.

Chloroform extract (11·20 per cent.) is colorless and slightly turbid. The residue, upon evaporation, is wax-like and hard (much resembling the residue from the ether extract). This residue is partially soluble in ether, and almost insoluble in alcohol and benzine. The aqueous washings from this extract give an acid reaction to litmus.

Acetone extract (5·98 per cent.) is of a yellowish color. The evaporation residue has a pungent, slightly aromatic odor and a dark brown color resembling the extract of plants. The residue is almost wholly soluble in alcohol, chloroform and amylic alcohol; but slightly soluble in ether, and insoluble in benzine.[13]

As the substances removed from the latex by volatile solvents were in the nature of material foreign to the enzyme, no systematic examination was made. These solvents do not seem to remove any proteid compounds save in the case of benzine, which extract gave a faint proteid reaction.

As a result of a rather hasty examination of these extractions, we may assume that they contain coloring matter; "vegetable extractive matter;" hard and soft waxes; hard and soft resins; a

[13] The alcoholic and acetone extracts give slight indications of the presence of nitrogenous matter by the soda-lime process.

volatile resin; a substance of the nature of fatty acids; pectose compounds.[14]

WATER SOLUBLE CONTENTS.

The dried latex extracted by repeated washings with water gives 82·74 per cent. of matter, soluble to a clear greenish-yellow solution. This watery extract is of acid reaction and responds to the usual tests for the presence of proteids, such as Millon's reagent; the xanthoproteic and biuret tests, etc.; precipitates are formed by alcohol, tannin, picric acid, platinum chloride, metaphosphoric acid, lead acetate, Mayer's reagent, mercury bichloride, potassium ferrocyanid and acetic acid. The presence of several forms of proteid substances is also shown by the following:

The filtered solution (noted above) is rendered turbid by heating to the boiling point. Upon continued boiling a very fine precipitate is separated, though this is not abundant. Filtering and further boiling produces no further precipitation, but the addition of nitric acid drop by drop gives a heavy flocculent precipitate. The clear aqueous extraction noted above, slightly acidulated with hydrochloric acid and heated, shows a slight turbidity just before reaching the boiling point. Cooling and the further addition of the acid produces at once a heavy flocculent precipitate, which dissolves upon heating and reappears upon cooling.

A solution of sodium carbonate (0·5 per cent.) added to the clear aqueous extract of the dried latex produces an immediate turbidity which, upon heating, separates into a small amount of fine precipitate. From these last results it will be seen that the soluble albumins of the latex of the papaw are only partially coagulated by heat.

When concentrated hydrochloric acid is cautiously added to the clear watery extract of the latex, there is formed a heavy curdy precipitate, soluble in an excess of the acid. In a clear aqueous solution of the latex, concentrated nitric acid produces a heavy

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[14] Malic acid has been noted as being present in the latex of the papaw. The acid principles of these extracts of the milk when subjected to the usual tests for malic acid, gave but slight indications of its presence.

The aqueous solution of the latex was examined at length and judging by the reactions noted in the text-books, and compared with malic acid itself, the conclusion was reached that no malic acid or malates were present.

white precipitate, also soluble in an excess of the acid (proteid reaction). This precipitate turns yellow and dissolves upon heating (albumose), but upon cooling is again precipitated. Upon adding an excess of acid it is completely dissolved and not re-precipitated when cooled (globulin).

The presence of soluble globulin in an aqueous solution is further shown in that the precipitate produced by boiling is not soluble in hydrochloric acid (0·2 per cent.).

The residue left upon the extraction of the dried milk with water

Water method of drying latex of papaw.

is partially soluble in a weak solution of common salt, and the resulting solution gives a precipitate with nitric acid (globulin).

The watery solution noted above, when rendered slightly acid (acetic) and boiled, is made turbid, forming small amount of flocculent precipitate (globulin and albumin).

The clear watery extract of the papaw latex, when saturated with ammonia sulphate, gives an abundant white precipitate with strong proteid reaction (the precipitate carrying the greater portion of the ferment). The precipitate just noted, freed from the ammonium sulphate, dissolved in water, made acid with acetic

acid, and then saturated with common salt, gives a white flocculent precipitate (primary albumose). After saturation with ammonium sulphate, the filtrate gives a precipitate, deutero-albumose, and the supernatant liquid, under the biuret test, shows the presence of peptones.[15] If precipitated by soda-magnesium sulphate, the filtrate likewise exhibits a strong peptone reaction.[16]

ANALYSIS OF PAPAW PROTEIDS.

It cannot be said that any of the enzymes have been completely isolated. The most that can be urged is that the enzymes are either proteid in character, or are associated with proteid bodies. In all, or nearly all, attempts to separate the enzyme from the accompanying proteid, the result has been a destruction of enzymic power. . Again, when in our manipulation of the enzymes we alter or destroy the character of the proteids which are associated with them, we alter or destroy the character of the enzyme. While it cannot be said that the enzyme and the proteid are identical, we must admit that the enzyme and proteid are most closely associated.

We have abundant authority to show that diastase is associated with leucosin; rennin is associated with hetero-proteose; bromelin appears in close relation to two forms of proteids, and so on through the list a close association of the enzyme with a proteid body can be shown. But it cannot be said that the proteid is actually the enzyme. So far as our present knowledge goes, an analysis of the proteid must stand for an analysis of the enzyme.

From the examination of the water-soluble contents of the latex of the papaw, we may reach the conclusion that the enzyme is associated with one or more of the soluble proteids. An analysis of these proteid bodies was therefore made, as follows:

For the purpose of analysis, a portion of the air-dried latex was extracted with alcohol, benzine and ether, to remove waxes, resins, etc., the residue consisting of the proteid matters and ash. This preparation is marked I in the accompanying table.

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[15] By the digestion of a solution of this peptone with the separated ferment or with trypsin, leucin and tyrosin appear (indicating hemipeptone).

[16] The classification of the albumoses and peptones is the subject of controversy. The classification here followed is that in most common use. Under another view we would have in this substance a mixture of globulin, proto and deutero albumose with, possibly, two or more forms of peptone.

A second preparation was made by extraction of the milk, as above, the product dissolved in water and the proteids precipitated by sodium chloride, and the precipitate partly freed from excess of salts, by dialysis:

This process was repeated with a view of obtaining an approximately pure preparation, and one representative of the enzyme of the latex. This preparation is marked II in the accompanying table.

PAPAW PROTEIDS.

	I. Per Cent.	II. Per Cent.
Air-dry.		
Carbon	39·96	42·81
Hydrogen	6·57	6·77
Nitrogen	11·26	10·09
Ash, or mineral matter	9·88	6·51
Moisture (loss at 100–105° C.)	10·83	7·90
Moisture-free.		
Carbon	44·81	46·84
Hydrogen	6·00	6·39
Nitrogen	12·62	10·95
Ash	11·07	7·06
Moisture-free, ash-free.		
Carbon	50·38	50·01
Hydrogen	6·74	6·87
Nitrogen	14·19	11·78
Oxygen	28·69	31·34
	100·00	100·00

The large proportion of mineral ash in the purest preparation—II—is notable and seems to indicate that the proteid constituents and the ash are most closely associated. Otherwise, we may observe that the carbon stands in about the same proportion as in other vegetable proteids. We have, however, a much smaller amount of nitrogen than is present in most proteids; but this low content of nitrogen is quite in accord with the constitution of some of the enzymes which have been examined. This is shown by the following comparison:

	Nitrogen. Per Cent.
Bromelin (Chittenden)	10·46
Trypsin (Kuhne)	13·41
Papaw (Kilmer)	11·78
Peptone (Henninger)	16·38

THE FERMENTS OF THE PAPAW.

The latex of the papaw is notable from the fact that it contains several soluble enzymes or ferments, or else (if such a thing is possible) a ferment body with a fourfold power. The ferments so far noted as contained in the latex are:

(1) A proteolytic ferment which decomposes proteids.

(2) A coagulating (rennet-like) ferment which acts upon the casein of milk.

(3) An amylolytic ferment having the power to attack starch, etc.

(4) A clotting ferment similar to pectase.

(5) A ferment possessing feeble powers of action upon fats.

The digestive action of the latex at the instant of its extraction from the green fruit is very marked. Placed in contact with such a substance as blood fibrin in a little water, the fibrin will be disintegrated before your eyes; mixed with milk and warmed, the milk is instantly coagulated. Boiled starch paste is thinned, and the blue color produced upon starch by iodine is changed to a purple in a few minutes. Poured over lumps of beef and placed in a warm place, the meat is softened, its fibres disintegrated, finally becoming a partially transparent jelly. The action upon cooked egg albumen is not so marked.

The latex when dried retains these powers in a somewhat lesser degree. I am of the opinion that the ferments exist in the latex, and possibly in the cellular structure, as a zymogen (carizymogen). This presumption is verified from the fact that after the extraction of the latex or pulp with water (preferably slightly acid or alkaline), a second maceration will bring a further yield of enzyme. I have repeated such a process ten times successively, in each instance bringing a further supply (small in amount) of the ferment into solution. If a considerable bulk of water (neutral, acid or alkaline) be added to the latex, and the resulting liquid be filtered and the residue on the filter paper washed with water, the greater portion of the ferment will be found in the filtrate.

The ferment may be extracted from the dried milk by water or glycerine (neutral, acid or alkaline), by very dilute alcohol (5-100); and from such a solution may be precipitated by any of the usual methods; such as an excess of full strength alcohol, saturation with alkaline salts, etc.

The following are the most important of the practical methods of separation. The first three are the methods of Peckholt:

(1) Exhaust the juice with ether; then exhaust the residue, first with absolute alcohol and next with 80 per cent. alcohol; the dried residue is then treated with water which dissolves it almost entirely, forming a turbid solution. The watery solution is finally precipitated with alcohol; the precipitate washed with alcohol, and dried over calcium chloride. Peckholt obtained by this process 7·848 per cent. of a white, light amorphous powder which he called "papayotin."

(2) Mix the juice with four times its weight of water; filter, and precipitate with alcohol (95 per cent.); wash and dry the precipitate. This gives 3·762 per cent. of a product practically the same as (1) but not quite so light.

(3) Evaporate the latex to dryness and then completely exhaust with ether and alcohol (absolute), as in the first method. Dissolve the residue in water and precipitate with alcohol. The result being a light brown powder of which Peckholt obtained 5·338 per cent. (He called this "parapayotin.")

(4) Wurtz prepared the ferment as follows: The milky juice was thrown on a filter and the coagulum washed with water. The aqueous solution then obtained was reduced to a small volume in a vacuum, and was precipitated by ten times its volume of alcohol. This precipitate was dried, dissolved in water and precipitated a second time with alcohol, washed with absolute alcohol and dried in a vacuum. The product of this process he called "papain."

(5) A method now in actual use in one of the West India Islands is as follows: Pour into the strained latex five times its volume of full strength alcohol, collect the precipitate and wash with absolute alcohol; dry over calcium chloride or sulphuric acid. (There is a considerable loss of alcohol; the product is small, fairly active, but high priced.)

(6) Method devised by the author: Dry the latex without heat; exhaust the dry residue first with ether, then with chloroform, followed by benzine; finally extract with alcohol. Under this process, if the extraction is thoroughly carried out, everything is removed except the proteids and ash. The product is a fine grey-white amorphous powder almost completely soluble in water, more active and more nearly representative of the peculiar properties of

the latex than the product resulting from any other method which has come under my observation.

(7) Salt-precipitation method. The well-known methods of precipitation by alkaline salts are applicable to the separation of the papaw ferments. The latex diluted with water or the dried latex extracted with water (filtered), when saturated with sodium chloride, with ammonium sulphate or with magnesium sulphate, will yield a heavy precipitate of the proteid contents carrying the greater portion of the ferments. Such precipitates may be freed from salts by subjecting their solution to dialysis, the resulting solution (and precipitated residue) are then to be evaporated to dryness.

The yield from these salt-precipitation methods is small, but, if the processes are carefully performed, furnish a satisfactory product, weaker however in action than those prepared by the method outlined in the preceding section.

Something like thirty methods for separation have been tried in my researches, with the result that all methods where precipitation is involved, tend to weaken the digestive power of the ferment. The methods used in the separation of pepsin whereby a purified and high power pepsin is produced, are as follows: Digestion of the proteid constituents, precipitation and purification of the product do not seem to be applicable to the papaw.

If the proteids of the papaw are digested by the aid of the contained ferments in either acid, neutral or alkaline fluids, and a separation and purification then made, the resulting product is decreased, and the digestive power is not increased; in fact, unless the process is most carefully performed, the absolute power of the ferment is greatly weakened.

It has been stated that the ferments of the papaw are chiefly associated with one of its proteid constituents.[17]

I have never been able to verify this statement. When any of the various forms of proteids are separated by the processes elsewhere outlined, heat or coagulation excepted, the separated body will be found to possess ferment power. Even the peptone remaining after separation of the albumoses exhibits feeble ferment powers. The ferment action seems to be the most marked when all of the proteids are associated together in their natural form.

(*To be continued.*)

[17] Martin believed the ferment to be associated with the proteid which he termed B Phytoalbumose.

THE "HOFMANN HAUS."

By H. V. Arny, Ph.D.

On October 20, 1900, the German Chemical Society dedicated, with appropriate ceremonies, the magnificent building erected in Berlin as a memorial to the great pioneer in the aniline industry and the famed teacher of chemistry, A. W. von Hofmann.

The building, designed as a home for the German Chemical Society and kindred organizations and as a hospice for sojourning foreign chemists, is located at Sigismundstrasse 4, and is a four-storied fire proof structure with a twenty-two meter front of Silesian sandstone, with two ornamental iron bow windows projecting from the second and third stories respectively, and with a red-tiled mansard roof. The ground floor is occupied by janitor's quarters and by a research laboratory. The second floor front contains offices of the society, while the third floor front is devoted to the library and committee rooms.

The rear part of the building is given up to an assembly hall, contains 254 seats arranged in tiers, rising level with the third story, the lecture counter being flush with the second floor. The top floors of the building are fitted up as offices and as store buildings. The entire edifice is lighted with electricity, contains an electric elevator and is heated with hot water. This structure and the lot on which it stands represents an expenditure of 575,000 marks.

A full account of the enterprise was contained in a special issue of the *Berichte* of the Society, published at the beginning of this year, and from it we can glean several lessons of value in the consideration of the proposed Procter Memorial. The figures will be given, as in the original, in German Reichsmarks, the equivalent in dollars being easily reckoned by dividing by four.

The financial commencement of the enterprise was the occasion of Hofmann's seventieth birthday, when his admirers raised a purse of 39,000 marks. Seven thousand marks of this was expended on a bust of the master; the remaining 32,000 marks being handed Hofmann as a jubilee purse. The recipient, with his characteristic generosity, augmented the amount with 8,000 marks of his own means and returned it to the committee with the request that it be called the Hofmann fund and used for the advancement of chemical science.

Hofmann died May 5, 1892, and immediately the German Chemical Society decided on a memorial to the eminent chemist, using the Hofmann fund, which, during the four years, had grown to 65,000 marks, as a nucleus.

The first call for subscriptions was dated November 12, 1892, and in response, 85,000 marks were subscribed by December 1st of same year. From then until October 1, 1893, 79,000 marks more were collected and during the ensuing fifteen months, up to January 1, 1895, additional subscriptions amounting to 12,000 marks were received. On May 12, 1896, three and a half years after issuance of the original appeal, the committee reported that the subscriptions and interest on same amounted to 176,000 marks.

The committee, having planned a memorial costing 800,000 marks, though sorely disappointed at the apparent failure of their hopes, renewed their efforts and succeeded during the next six months in bringing the fund up to 229,000 marks.

In December, 1896, they purchased a site for the building for 275,000 marks, covering the deficit by drawing on the original Hofmann fund. They then formed a stock company, capitalized for 300,000 marks, for the erection of the building, issuing bonds of 5,000 and 10,000 marks value, bearing 3½ per cent. interest. These bonds were bought by German chemical corporations and others, and of the 300,000 marks thus subscribed, bonds amounting to 140,000 marks were returned to the corporation, all claims of payment of both principal and interest being waived by the generous subscribers, on occasion of the dedication of the building.

This leaves a debt of 160,000 marks, secured by a mortgage on the property, and which it is hoped will be paid off by legacies. One such has been announced—Commercienrath J. F. Holtz, Treasurer of the German Chemical Society and the most indefatigable member of the memorial committee, having expressed the intention of giving 30,000 marks.

The interest on the bonds will be met by the rental on the property paid by the several organizations having their home in the building.

An analysis of the subscription list may prove interesting.

The total amount, 236,751 marks, was obtained from 1,350 subscribers, whose gifts ranged from 20,000 marks to 50 pfennig (12 cents); 244 contributors furnishing 221,850 marks.

The several large donations are as follows, the names of the donors known on this side of the water being given in brackets. These do not include the cancelled bonds of 10,000 and 5,000 marks each, total 140,000 marks contributed by nineteen persons. Besides these there were two gifts of 20,000 marks each, from two dyestuff corporations; one of 10,000 marks, four of 6,000 marks (Fahlberg and Tiemann); six of 5,000 marks; five of 3,000 marks (Bayer of Elberfeld); two of 2,500 marks, eight of 2,000 marks (Bayer of Elberfeld, Schering of Berlin, Fischer of Berlin); eight of 1,500 marks (Schering); twenty-seven of 1000 marks (German Soda Works, German Solvay Works, German Explosive Works, Kalle of Biebrich, Knorr, Pintsch and Siemens of Berlin); two of 800 marks; five of 600 marks; thirty-one of 500 marks; four of 400 marks; fourteen of 300 marks; five of 250 marks; twenty-nine of 200 marks, and ninety of 100 marks. It may be interesting to note that a collection was taken up in practically every chemical laboratory in Germany, thus giving each student an opportunity of contributing his mite.

Among special contributions not enumerated above may be mentioned a gift of 7,000 marks for fitting up the library, from Professor Harries of Berlin; a large number of books and apparatus from various German firms in that line of business; a marble statue of Hofmann, for which fifty-seven subscribers donated 14,475 marks; and Hofmann's library, given by his widow.

In conclusion, it will be seen that the raising of funds necessary for so expensive a structure as the "Hofmann Haus" was accomplished only after herculean efforts, it taking eight years to collect 376,000 marks and even then there is left a debt of 160,000 marks. Let those in charge of the Procter Memorial bear this in mind and let them therefore plan more moderately than did their German confrères.

On the other hand, if the German chemical interests freely gave 236,000 marks for a memorial possessing largely the nature of a club house; there seems no reason why the American drug trade should not raise $50,000 for an undertaking of such far-reaching importance as a research laboratory.

PUMPKIN SEED OIL.

By Willard Graham, P.D.

Pumpkin Seed Oil as found in commerce varies in quality and is generally, if not always, obtained by the use of a solvent. The expressed oil is not used to any great extent, as the extracted oil is cheaper.

A quantity of whole seeds were ground and extracted with acetone; the acetone being recovered by distillation. The yield was 25 per cent. of an oil having the following properties:

A clear reddish limpid liquid having an agreeble odor and taste, a specific gravity of 0·9208 at 15° C., saponification number 192·5, acid number 18·9, ether number 173·6, soluble in all proportions of carbon disulphide, ether, chloroform and in twenty parts of absolute alcohol, drying on standing to a tough yellowish transparent mass.

A commercial oil was obtained and on examination gave the following results:

A clear reddish liquid of an agreeable odor and taste, having a specific gravity of 0·9197 at 15° C., saponification number 195·2, acid number 3·5, ether number 191·7, soluble in all proportions of carbon disulphide, ether, chloroform, and in twenty parts of absolute alcohol.

The above oils having been obtained by extraction it was deemed desirable to examine an oil obtained by expression, but after subjecting a quantity of ground seeds to a pressure of 3,000 pounds, no appreciable quantity of oil was secured on account of the porous condition of the seeds.

Benedikt and Lewkowitsch in their "oils, fats and waxes" describe it as an oil expressed from the seed of *Cucurbita Pepo*, specific gravity at 15° C., 0·9231, saponification number 188·1, iodine value 121, solidifying point—15° C., melting point of mixed fatty acids 28° C.

Carvone Content of Volatile Oils.—According to Kremers (*Jour. Soc. Ch. Ind.*, January 31, 1901,) the determination of the carvone content of volatile oils, containing this ketone, as carvoxime, while by no means perfect, is unquestionably a step in the right direction, the one great advantage being that a definite crystalline compound is weighed.

THE LLOYD REACTION FOR MORPHINE.[1]

By Joseph L. Mayer, Phar.D.

Contribution from the Chemical Laboratory of the Brooklyn College of Pharmacy.

Since the publication of the installment of Professor Lloyd's "Stringtown on the Pike," which had to do with the trial scene, tests and results, the journals have contained in almost every issue contributions which in one way or another relate to the well-known bichromate-sulphuric, strychnine reaction.

Prominent among those who have contributed articles on the subject is Mr. Seward Williams, who in the April number of the *Druggists Circular* elaborates his previous discussion concerning the possibility of mistaking a morphine-hydrastine mixture for strychnine.

He concludes that "the moral of the story is not to place too much reliance on any one of the generally recognized evidences of organic poisons."

In going over the reactions he finds that the morphine-hydrastine mixture with a few drops of concentrated sulphuric acid, will, even in the absence of potassium bichromate, produce the violet-blue color which so nearly simulates the characteristic strychnine reaction that Professor Lloyd yielded to the temptation to make it the theme of one of the most powerful climaxes of his deservedly popular novel.

As a consequence Mr. Williams proposes that "we shall add to our list of alkaloid color-tests the two just mentioned and know them as the Lloyd reactions for morphine and hydrastine, if agreeable to Professor Lloyd."

If the unknown substance is suspected to be morphine, add a small a mountof hydrastine and a few drops of concentrated sulphuric acid; a violet-blue color appearing after five minutes indicates morphine.

If hydrastine is suspected, add to the sample a small amount of morphine and a few drops of concentrated sulphuric acid; a violet-blue color after five minutes indicates hydrastine.

As a matter of fact, modern methods followed in toxicological

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[1] Read at the annual meeting of the New York State Pharmaceutical Association, June 4-8, 1901, and communicated by the author.

analysis have so taken advantage of the solubility of the alkaloids in the solvents employed in their separation, that even if some color reactions are common to several alkaloids, unless these alkaloids are separated in the same step in the examination, the chances of error are minimized.

It is the possibility of making an error that emphasizes the necessity of having an unlimited number of tests of identity. Experiments recently made, prove that chloroform will dissolve out of a solution sufficient morphine and hydrastine to react violet-blue with concentrated sulphuric acid and potassium bichromate.

While it is true that the reaction differs from that obtained with strychnine in persisting some time, instead of being evanescent, it is plain to see how a mistake might easily be made.

Had "Professor Drew," the chemist in "the Stringtown poisoning case," been more observant, and applied other tests than the bichromate one, his testimony would not have supplied the powerful link it did, in the prosecution's strong chain of circumstantial evidence. Tests of identity and confirmatory ones are not only necessary in examinations of this character, but are required by the pharmacist to enable him to identify the alkaloids he purchases and dispenses. For example, the United States Pharmacopœia requires that quinine "should not produce a red color with nitric acid (difference from morphine)."

These facts suggested to the writer, that if hydrastine when mixed with any alkaloid other than morphine, in the presence of concentrated sulphuric acid, after five minutes' stirring failed to produce the violet-blue color, the reaction would be a valuable addition to the tests for differentiating morphine from other alkaloids.

The following are the results of the experiments I made to determine this question.

The conditions and method of applying the tests were alike throughout, and consisted in mixing approximately one part of hydrastine with eight parts of the other alkaloid.

After the addition of a few drops of concentrated sulphuric acid the mixture was stirred with a glass rod for at least five minutes. In view of the fact that many alkaloids give colorations for the first few minutes which are totally different from the end reaction, the direction to "stir at least fives minutes" must be strictly observed.

The alkaloids operated upon, those most likely to be found in the drug store were the purest obtainable.

The following table gives the colors produced by stirring the alkaloids named with hydrastine and concentrated sulphuric acid for five minutes:

Aconitine	Brown.
Atropine	Pinkish.
Berberine	Greenish-brown.
Brucine	Light-brown.
Caffeine	Dirty-white.
Cinchonine	Dirty-yellow.
Cinchonidine	Dirty-white.
Cocaine	Unaffected.
Codeine	Pinkish.
Digitaline	Mahogany.
Heroin	Violet to purple.
Homatropine	Pale-yellow.
Hyoscyamine	Dirty-white.
Morphine	Violet-blue.
Pilocarpine	Light-brown.
Quinidine	Light-green.
Quinine	Greenish-yellow.
Sparteine	Greenish-yellow.
Strychnine	Dirty-white.
Veratrine	Royal purple.

An analysis of these results shows that but three out of the twenty samples examined give a violet-blue color under the above conditions, viz., heroin, morphine and veratrine.

Among this number only one gives a cherry-red color with cold concentrated sulphuric acid, viz., veratrine.

The remainining two are differentiated by nitric acid; an orange-red color indicates morphine and a yellow color heroin.

When we consider the sharpness of the reaction with the simplicity and ease of application, it becomes apparent that Lloyd's test for morphine is one worthy of a place among the alkaloidal color reactions.

Fully realizing the importance attaching to the necessity of subjecting as many alkaloids as possible to the test, the writer regrets exceedingly that the number at his disposal was so limited, but hopes in the near future to report on those not included in the present work.

THE ANISEED OILS, AND ANETHOL.[1]

By George R. Pancoast, M.D., and Lyman F. Kebler, Ph.C.

Aniseed oil is one of the oldest of essential oils known, having been observed as early as the sixteenth century. On account of its being a grateful aromatic and a mild carminative it has received general recognition by the various pharmacopœias. The 1880 U.S.P. recognized, and the 1898 Br. Phar. at present recognizes, both the oils distilled from Anise and Illicium. The former states that Oil of Illicium has nearly the same properties as oil of Anise, except that it congeals at about 2° C. while the latter recognizes a difference in the solubility in alcohol. The 1890 U.S.P. recognizes only the oil distilled from *Pimpinella Anisum* L. (Nat. Ord. Umbelliferae). Why this restriction has been made is not apparent. The plant originally came from Egypt and the Levant, but on account of its usefulness, importance, and ease of production, it is now cultivated in nearly all parts of the world. Russia at present is the largest producer of oil, not solely because it grows the greatest quantity of seed (about 3,000 tons annually) but rather because the seed is of inferior quality and is of little value except for oil. Spain has of late years produced about 1,500 tons per annum, and Turkey not far from this amount; but these two countries produce large, pure seed of such fine quality as to commercially preclude its use for oil.

Seed from various sources will yield from 1½ to 6 per cent. of oil. In some localities, stems, chaff and even the leaves are added to the fruit before distillation. Chaff yields about ½ per cent. of oil.

The physical properties of aniseed oil have been thoroughly investigated and are as follows; at, or above 20° C. it is a colorless or pale yellowish, strongly refractive liquid, of a characteristic odor and sweetish, mildly aromatic, taste. At or about + 15° C. it solidifies into a snow-white crystalline mass, called by some "flat tablets" and again becomes completely liquid at from + 18 to + 20° C. An oil that requires a temperature below + 15° C. for congealing should be looked upon with suspicion. The specific gravity of a fresh oil is 0·980 to 0·990 at 17° C. increasing with age; due to the

[1] Read before the Pennsylvania State Pharmaceutical Association, June, 1901, and communicated by the authors.

formation of anisaldehyde, anisic acid and polymeric anethols. The plane of polarized light is turned slightly to the left up to 1° 50 minutes. It is clearly soluble in an equal volume of alcohol and the resulting solution should not assume a blue or brown tint on the addition of a drop of solution of iron chloride (absence of phenol). With age the oil becomes more readily soluble in alcohol.

The principal constituents are anethol, 80 to 90 per cent., and methylchavicol, an optically inactive body having the odor of aniseed oil, but lacking its sweet taste.

For the various adulterants found from time to time and methods of detecting the same, see a former paper by the authors, in AMERICAN JOURNAL of PHARMACY, 73, 1, entitled "Adulterations of Essential Oils."

Before taking a sample for examination, the contents of the can should be thoroughly liquid and well agitated so as to get a representative sample.

Aniseed oil, it is said, can only be distinguished from star anise by the odor and taste. Various other distinguishing tests have been suggested, but none have proved satisfactory. It is probably due largely to the close similarity of the two oils, and the difference in price, that the former has been largely displaced by the latter; which is derived from the fruit of Illicium verum, H. (Nat. Ord. Magnoliaceae). The new German Pharmacopœia has met the existing conditions very well in that it recognized neither of the oils, but their chief constituent, anethol. Whether such a step is a good one, time alone can tell.

Star anise oil is practically controlled by the Chinese. At the source of distillation it is placed into tin cans holding from 32 to 35 catties (42 to 46 pounds) and shipped to Hong Kong or other prominent markets, from whence it is sent out in lead canisters holding 7½ kilos. Some of the star anise oil is sent through Tonquin, the French centre of distribution. The construction of the canisters is not the most convenient, for readily emptying, without loss. The following precedure works very satisfactorily. Cut a round hole into the centre of the canister, through the seal, make this opening perfectly smooth and round by means of a reamer; into this opening insert a double perforated cork, carrying in one opening a siphon-shaped glass tubing, of suitable size and length, armed with a piece of rubber tubing at both ends, the rubber piece inside the container is about an inch long, and the one outside a foot

long. Into the other opening insert a straight glass tube. The apparatus is now ready for use. Slightly elevate the canister, place a receiver under the long rubber tubing and start the siphon by blowing into the short glass tube. The canister is thus quickly emptied without loss. The small quantity of oil remaining, can readily be removed by draining.

The physical properties of this oil are about the same as those for aniseed, the slight variations having been noted above.

The composition of star anise oil appears to be somewhat more complex than that of anise oil.

Many adulterants have been reported by the various investigators, but at present only those of a more scientific character are met. Kerosene seems to have been used largely at one time, but the writers never met with any in this oil. It might be interesting, however, to record a few observations made with this adulterant.

Schimmel's Report, April, 1897, p. 38. contains the following:

	Specific Gravity at 15° C.	Congealing Point.	Solubility in alcohol.
Pure Oil	0·986	+ 18° C.	Soluble in 2·2 and more parts
Oil + 5 per cent. kerosene	0·978	+ 16¼° C.	Not soluble in 10 parts
" +10 " " "	0·970	+ 14¾° C.	" " " "

J. C. Umney reported the following observations; *Chem. and Drug.*, Vol. 51 (1887), p. 623:

	Specific Gravity at 15° C.	Congealing Point.	Contained.
1	0·894	+ 5·7° C.	56 per cent of Kerosene
2	0·926	+ 9·7° C.	37 " " "
3	0·939	+ 11·5° C.	36 " " "
4	0·920	+ 8·8° C.	41 " " "
5	0·910	+ 7·8° C.	47 " " "

The above data were obtained from star anise oil of the London market.

The authors have recently examined a number of samples of the various aniseed oils offered as pure, with the following results:

	Source.	Specific Gravity.	Optical Rotation.	Congealing Point.	Solubility in equal volume of alcohol.
1	Russian	0·9838 at 17° C.	+ 3° 50′	+ 15° C.	Soluble
2	"	0·9893 " 20° C.	— 4° 59′	+ 18° C.	"
3	Tonquin . . .	0·9834 " 17° C.	— 1° 30′	+ 17° C.	"
4	Star Anise . .	0·9648 " 17° C.	— 1° 27′	+ 15° C.	"
5	" . .	0·9870 " 17° C.	+ 0° 58′	+ 16° C.	"
6	" . .	0·9822 " 17° C.	— 1° 53′	+ 15.5° C.	"
7	" . .	0·9821 " 17° C.	— 1° 31′	+ 14·5° C.	"
8	" . .	0·9832 " 17° C.	— 1° 44′	+ 14° C.	"
9	" . .	0·9832 " 17° C.	— 1° 44′	+ 14° C.	"

Oils Nos. 1 and 2 have undoubtedly been tampered with. The disturbed optical rotation of No. 1 is probably due to added oil of fennel, or some of its derivatives. What the disturbing factor of No. 2 is, the authors are unable to conjecture. No. 8 is also abnormal, due probably to the same added impurities as No. 1, or possibly added star anise leaf oil, which has a specific gravity of 0·9878 at 15° C. and an optical rotation of + 1°. The anethol content of star anise leaf oil is small, and the congealing point correspondingly low. It has been called "Liquid star anise oil" and has no practical value, except as an adulterant.

Oils are occasionally met with, having a low congealing point, yet are not adulterated. These are the "Flower Oils." They are obtained from a mixture of natural and artificially ripened seeds; *i. e.*, the branches are gathered before the fruit is all ripe so as to hasten the ripening of the green seeds. Such oils cannot be considered equal to an oil made entirely from prime seed.

ANETHOL.

The present German Pharmacopœia describes anethol as a colorless, highly refractive liquid, of a pure anise odor, and of intensely sweetish taste; specific gravity at 25° C. 0·984 to 0·086; melting point, + 20° to + 21° C.; boiling point 232° to 234° C. and must form a clear solution with two parts of alcohol.

Several samples examined by the writers yielded:

	Specific Gravity.	Optical Rotation.	Congealing Point.	Boiling Point.
A.	0·9895 at 20° C.	inactive	+ 17° C.	210–235° C.
B.	0·9896 at 20° C.	— 1° 30′	+ 20° C.	220–235° C.
C.	1·0525 at 15° C.	— 2° 18′		228–245° C.
D.	0·9870 at 20° C.	+ 5° 22′	+ 20° C.	229–236° C.
E.	0·9847 at 20° C.	inactive	+ 19° C.	210–235° C.

All are soluble in an equal volume of alcohol. A, B and E are of fair quality and comply fairly well with the above requirements, but anethol is generally considered optically inactive. C and D were labeled liquid anethol. We are informed that this is a redistilled oil of anise, prepared from the regular anise oil of the market. Liquid anethol is therefore a misnomer. It is desirable here to remark that C was an old sample and its original physical properties may have changed. D appears to be "anethol" derived from oil of fennel.

Laboratory of Smith, Kline & French Co.

CORRESPONDENCE.

WOOD ALCOHOL.

Editor AMERICAN JOURNAL OF PHARMACY:

Permit me a word on the use of wood alcohol for heating purposes, spoken favorably of in a recent number of the JOURNAL. Unquestionably methyl alcohol is a cheaper fuel than grain spirit. It costs less and generates, weight for weight, more heat. However, its use is attended sometimes with inconveniences that must be taken into consideration. From its greater volatility it is even more dangerously inflammable than ordinary alcohol. On account of this volatility, also, there is much greater waste in its use, the loss from evaporation in storing being more considerable and control of the rate of combustion in ordinary spirit lamps being more difficult.

When burned in the safety spirit lamps, in which the fluid is absorbed by asbestos covered by brass wire gauze, the metal of the gauze is rapidly corroded, as shown by the deep green or blue color imparted to the flame, and a brass kettle heated over the flame becomes quickly tarnished. As a fuel, therefore, for use at the tea table, wood spirit cannot be recommended, at least where brass utensils are employed.

A. B. LYONS.

PROCTER MEMORIAL.[1]

In response to a letter from the Editor of this JOURNAL concerning the feasibility of establishing a Research Laboratory as a memorial to the life and work of Prof. William Procter, Jr., by the American Pharmaceutical Association at its semi-centennial in 1902, the following are some of the replies which have been received:

DEAR SIR:—In a former communication I expressed the idea that some monument in memory of William Procter, Jr., would be the most appropriate memorial of his life and work. If he could have been consulted about the matter he would have said, "Let it be a Research Laboratory," and so, perhaps, we owe something to his known preferences. If the necessary funds can be obtained and arrangements made for the permanent maintenance of a research laboratory, it seems to me it would be a most fitting monument to

[1] For other information and correspondence on this subject, see November, 1900, and February, March, April, May and June issues of this JOURNAL.

his memory. I can see a number of difficulties that will have to be overcome in the conduct of such an establishment, but without doubt these can all be overcome.

The Faculty and Directors of the Philadelphia College of Pharmacy would, it seems to me, be the proper persons to be entrusted with the carrying out of this project by reason of his association with its early history, and Philadelphia being the city in which his life-work was done; and I see no reason why a national monument should not, in this way, be cared for by the mother of all the colleges in the United States.

W. M. Searby.

San Francisco, Cal.

Dear Sir:—Replying to your letter of April 4th, in which you state that it may be possible to establish a research laboratory at the fiftieth anniversary of the A.Ph.A., I have to say that I am greatly pleased at this outcome of the discussion, and if there is anything I can do to further the scheme by encouraging sentiment in favor, I should be very glad. I hope that the research laboratory will include various kinds of pharmacological work, will not confine itself to strictly chemical study, but will embrace physiological pharmacology, which has grown to be so important to the physician especially, but to the pharmacist as well.

Anything that we can do in this laboratory on the broad lines of medical and pharmaceutical science for the benefit of human society, should meet with hearty approval, and should have the co-operation of all interested in medical science in any of its branches.

L. E. Sayre.

Lawrence, Kan.

Dear Sir:—Your agreeable communication of recent date, relative to the project of a *Procter Memorial*, and asking for an expression of opinion thereon, has been duly considered, and we beg to state as follows:

Believing, as we do, in a glorious future for American pharmacy, and in the eminent value of the instrumentality of the American Pharmaceutical Association in promoting that consummation, we quite agree with the proposition conveyed in your editorial in the American Journal of Pharmacy of November last, that the fiftieth anniversary of the Association be commemorated by some act of

historic significance, worthy and expressive of the high mission of that organization.

Recognizing also the distinctive prominence of the late Professor Procter as a pioneer, guide and leader in the evolution of pharmaceutic science and practice on this continent, we deem it likewise proper that the above-indicated commemorative act should bear his name and thereby serve to perpetuate and honor his memory.

As to those forms suggested for this Memorial, on the feasibility of which no doubts have been expressed, we incline to side with the view variously supported in your correspondence columns, that neither the Statue nor the Medal plan would be sufficiently reminiscent of the modest bearing, assiduous toil, and self-denying devotion to a noble cause, which characterized the great pharmacist whom it is desired to honor. In what we are informed to have been *his* spirit, the General Scholarship plan would, among the admittedly practicable suggestions so far put forth, appear to us to claim first place.

MERCK & CO.

NEW YORK CITY.

DEAR SIR:—Replying to your esteemed favor of the 5th inst., relative to "memorializing the life and work of Prof. William Procter, Jr.," it seems to me we should try to combine sentiment with utility. Sentiment, to satisfy the desires of the heart towards one we love and have lost, and utility, to perpetuate the memory of the departed.

In the lecture room, where he was wont to teach, to give up the best part of the results of his untiring labors among those he loved and was loved by—there, where the happiest and best years of his life were spent, let there be erected a beautiful white marble tablet, bearing "en relief," a bronze (bust size) profile, elegantly done—true to life—with a proper dedication embodying his worth as a man, pharmacist and friend; also the affectionate regard of those (students, etc.) erecting said tablet—so much for the sentiment portion—a just tribute to a great and good man, upon the spot of his well-earned honors.

Now, as to the utility portion—every year, let there be conferred, jointly by members of the A.Ph.A. and Philadelphia College of Pharmacy—a free tuition, in the name of Prof. William Procter, Jr., for the degree of pharmacist (Ph.G.) in the Philadelphia College of

Pharmacy, upon some worthy lad who lacks the means. * * * I think Prof. William Procter, Jr., would have been well pleased with this.

The research laboratory idea is all right, but it had better be left to those with unstinted means; this is more a labor of love than vain glory and should be made up of contributions like unto the widow's mite.

We want something simple, impressive and lasting, dignified and true to the purpose. Anything involving a large expenditure will either not be realized or only create an opening for would-be geniuses. Prof. William Procter, Jr., and his memory would be lost in the refulgence cast by the halos around the heads of "Research Laboratory" workers.

Let us love and honor the man for his many cardinal virtues, but in such a way that his, and only his, memory get the full benefit. I have no use for these double-edged schemes, which are like unto the Spanish proverb which says: "He who asks for God, asks for two." (A reference made to the pious monks asking charity.)

BROOKLYN, N. Y.

E. FOUGERA.

RECENT LITERATURE RELATING TO PHARMACY.

BACTERICIDAL ACTION OF PAINTS.

Cultures of various pathogenic bacilli—such as those of diphtheria, cholera and typhoid—transferred to freshly painted surfaces of wood, tinplate and earthenware, and observed under various conditions of time and temperature, were destroyed in every case, as shown by the inability to produce new cultures from the experimental material. That the destruction was not due to chemicals was shown by the fact that the same cultures thrived in 1 per cent. solutions of magnesium chloride and of arsenous acid.

The writer, noting that linseed oil paints were the best germicides and also that all such paints, on drying, react to ozone paper, concludes that the antiseptic action of paints is due to the formation of ozone in the oxidation of drying oils. (M. Piorkowski, *Bericht. dtsch. Ph. Ges.*, 1901, 85).

H. V. ARNY.

FUNGICIDAL ACTION OF VOLATILE OILS.

Interesting to compare with above is an article by T. Borkorny (*Ph. Cent.*, 1901, 159, and 172) in which he reports elaborate experiments on the destruction of mould (Schimmelpilz) and putrefaction bacteria with ethereal oils and their derivatives, drawing therefrom interesting conclusions as to chemical structure and relative toxicity. Quoting Loew's classification of toxicological action, in which he assumes that death of organisms by poison is due to the chemical decomposition of the protoplasm—be it by complete dissociation, or by formation of substitution products.

The writer cites the following oils as most toxic to mould, deducing the reason for toxicity from their chemical structure.

First comes *eugenol*, a phenol, and all phenols form substitution products with the protoplasmic constituents. It likewise contains an allyl group—$CH = CH_2$, and all unsaturated groups are more poisonous than the corresponding saturated body. Thus allyl mustard oil is much more toxic than ethyl mustard oil. Second in antiseptic nature is *cinnamic aldehyde*, $C_6H_5CH = CH\ CHO$, which is toxic because of its CHO group. Aldeyhdes are more toxic than their corresponding alcohols (note antiseptic action of formaldehyde, as compared to its congener, methyl alcohol) because, according to Loew, they react with the amido groups found in the protoplasm. Cinnamic aldehyde, moreover, contains the unsaturated group—$CH = CH$—which contributes to its toxic action. *Salicylic aldehyde*, C_6H_4CHO, is more toxic to fungi than its alcohol, saligenin, or its oxidation product, salicylic acid, again showing influence of the aldehyde group. Lastly, all bodies containing the phenyl group, C_6H_5, show more toxic character than corresponding substances of the marsh gas series. H. V. A.

CLARIFICATION OF ALBUMINOUS URINE.

The clearing of urine prior to testing for albumin is sometimes difficult, and such foreign bodies as magnesia, aluminum hydrate, red lead or talc, have been recommended for the purpose. All, however, carry down considerable albumin, hence are not advised. Infusorial earth is the least objectionable clarifying agent, and even this should be used in small amounts only, not exceeding ½ per cent. After all, shredded filter paper is the most reliable clarifying agent.—(Dr. Grützner, *Ph. Zt.*, 1901, 78.) H. V. A.

POISONOUS STAR ANISE.

C. Hartwich (*Schw. Wochenschr. Ch. und Ph.*, 1901, 107) finds star anise of Swiss commerce contains 10 to 20 per cent. of the poisonous fruit of Illicium religiosum. He calls attention to the means of detection suggested by Lenz. (See this JOURNAL, 1900, 75). H. V. A.

REVIEWS AND BIBLIOGRAPHICAL NOTICES.

A HANDBOOK OF MATERIA MEDICA, PHARMACY AND THERAPEUTICS, including the posological action of drugs, the special therapeutics of disease, official and practical pharmacy, and minute directions for prescription writing. By Samuel O. L. Potter. Eighth Edition, Revised and Enlarged. Philadelphia: P. Blakiston's Son & Co. The new edition contains 950 pp. octavo. Price, in Cloth, $5 00; in Sheep, $6.00.

This well-known, comprehensive and commendable work has again been subjected to a thorough and critical revision, has been largely rewritten, and has been expanded by the introduction of much new matter. The latter has to some extent taken the place of material considered obsolete or comparatively unimportant, so that the increased size of the book over the previous edition is only twenty pages.

In the section on Materia Medica the following articles have been rewritten: Argentum, Cinchona, Coca, Coffea, Digitalis, Dulcin, Ergot, Ferrum, Ipecacuanha, Myrrha, Saccharinum and Veratrum Viride. The new matter includes paragraphs on Actol, Airol, Argentamin, Argentol, Argonin, Chinosol, Creosotal, Dionine, Eucaine, Eudoxin, Glycero-phosphates, Heroine, Holocaine, Iodothyrin, Itrol, Largin, Nesophen, Orphol, Orthoform, Passiflora, Pellotine, Peronine, Phloridzin, Piperidin, Protargol, Tuberculin-R, Urotropin and Xeroform.

In the section on Therapeutics new articles are inserted on Local Anesthesia, Beriberi, Dhobie Itch, Tropical Fevers, Heat-stroke, Hemoglobinuric Fever, Lymphadenoma, Miliaria, Bubonic Plague, Sprue, Tinea Imbricata, Tinea Versicolor and Toxemia. Twenty-eight articles in this portion of the book have been rewritten, including those on Amenorrhea, Asthma, Boils, Cholera, Diabetes, Dysentery, Dyspnea, Gonorrhea, Insomnia, Leprosy, Leucocythemia, Lichen, Myxedema, Pemphigus, Phthisis, Remittent Fever, Typhoid

Fever, Septicemia, Shock, Suppuration, Ulcers, Uremia, Variola and Wounds. The text of many other articles has been expanded by the incorporation of more than two hundred items from current medical literature and from the author's personal experience in practice. The articles on Poisoning, on Temperature in Disease, and on the Clinical Examination of the Urine have been transferred to this part of the book from the Appendix, in the belief that they will be more frequently consulted when found in their alphabetical order in the section on Therapeutics.

Potter's Handbook is one of those works that contains a vast amount of information and is teeming with the results of the author's own personal experience and operations. The present edition contains material gathered from the writer's experience in active professional practice in a tropical climate, among soldiers and civilians, men, women and children, during a period of nearly two years' duration. The book is of great value to medical students and physicians and will be found also a valuable reference book by pharmacists and dentists as well.

Merck's 1901 Manual of the Materia Medica. A ready reference pocketbook for the practising physician and surgeon. Compiled from the most recent authoritative sources and published by Merck & Co., New York and Chicago.

This handy little book of nearly 300 pages contains a vast amount of information regarding the physical and chemical properties, physiological effects and therapeutics, uses of drugs, as well as a formulary of well-selected prescriptions and a valuable article on poisoning and its treatment. It will be found invaluable to the busy practitioner and is in just such a form that it may be carried about in the pocket and readily consulted.

Memoranda on Poisons. By Thomas Hawkes Tanner. Eighth revised edition by Henry Leffmann. Philadelphia: P. Blakiston's Son & Co.

This little book will be of value not only to physicians, but also to pharmacists. It contains concise information regarding the diagnosis and treatment of poisoning and many other features connected with this subject. The handy compact form of the book will make it useful, particularly to students and young practitioners of medicine, as well as pharmacists who occasionally are called up to assist in the saving of life until the physician arrives.

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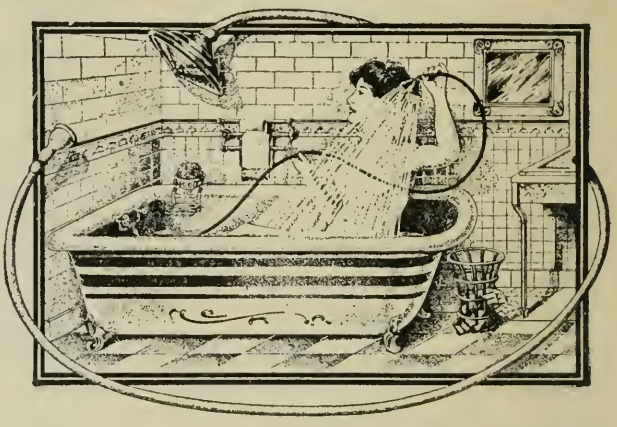

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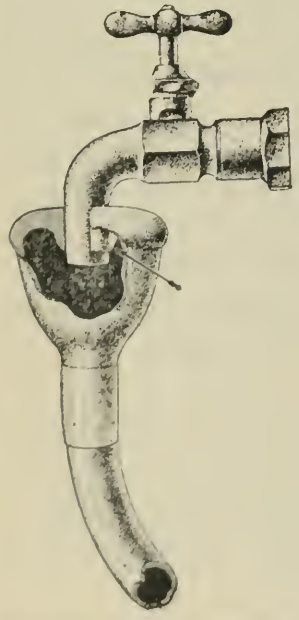

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